REMARKS

STATUS OF THE CLAIMS

Claims 1 – 5 and 7 – 13 are pending in the application. Claim 6 was previously canceled. Claim 1 is amended. The amendments to claims 1 and 10 are made to correct obvious typographical errors. Therefore, no new matter is presented.

Reconsideration and re-examination of this application in view of the following remarks is hereby respectfully requested. Applicant wishes to thank the Examiner for the reconsideration and withdrawal of: (1) the prior rejection of claims 1-5 and 7-13 under 35 U.S.C. 112, first paragraph for allegedly lacking written description; and (2) the rejection of claims 1-5 and 7-9 under 35 U.S.C. 103(a) as allegedly being unpatentable over Biskobing with WO 97/32574 in view of Halonen et al. (U.S. Pat. No. 6,245,819) further in view of Vasu and Melander et al.

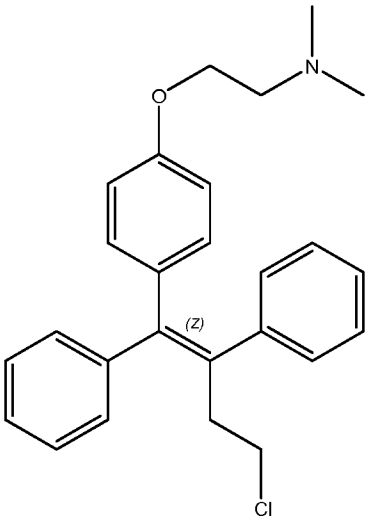
I. REJECTION UNDER 35 U.S.C. §102(b)

Claims 1 and 3-5 stand rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Anttila, *Head & Neck Cancer*, 1997 Abstract Number 1144 ("Anttila"), as evidenced by Kangas, *Cancer Chemotherapy and Pharmacology*, 27:8-12 (1990) ("Kangas"). Applicant respectfully traverses.

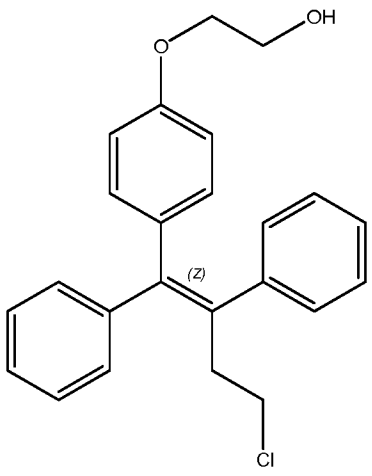
The Examiner argues that Anttila discloses administering 60 mg/day of a *metabolite* of toremifene with food to healthy male volunteers. This is incorrect. Anttila discloses the oral administration of toremifene citrate, not a metabolite thereof, to 12 young, healthy male subjects. A single, 60 mg dose of toremifene was administered once after a 14-hour fast, and once following a standard high-fat meal. Serum samples were obtained periodically, 0-28 days post-dose. Serum levels of toremifene and its metabolites were determined using an HPLC method.

In short, only toremifene (in its citrate salt form) was administered to the subjects. The serum levels of toremifene and its metabolites were measured after administration of the toremifene. Anttila does not disclose the administration of any metabolite of toremifene.

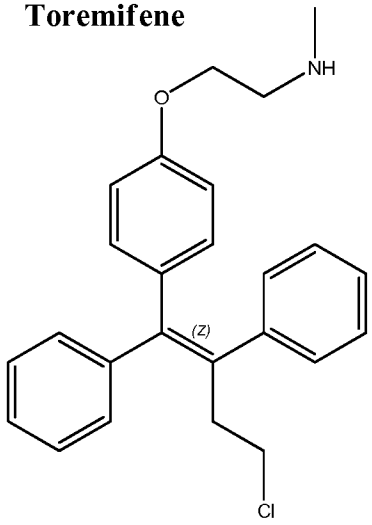
Claims 1 and 3-5 of the claimed invention all require that ospemifene be administered. Ospemifene is structurally different from toremifene. The structure of ospemifene is compared to toremifene and N-demethyl toremifene:



Toremifene



Ospemifene



N-demethyltoremifene

Since Anttila does not teach the administration of ospemifene to its subjects, it does not anticipate claims 1 and 3-5. Therefore, Applicant respectfully requests that the rejection of claims 1 and 3-5 under 35 U.S.C. 102(b) be reconsidered and withdrawn.

II. REJECTION UNDER 35 U.S.C. §103(a)

Claims 1-5 and 7-13 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over Anttila in view of U.S. Pat. No. 6,984,665 ("Blom et al."). This rejection is respectfully traversed.

As stated above, the Examiner misinterprets the Anttila reference. The Examiner mistakenly believes that Anttila teaches the administration of a metabolite of toremifene. Anttila teaches the administration of toremifene, not ospemifene. The Examiner uses Blom et al. to teach ospemifene, the claimed doses, and the uses of ospemifene for treating osteoporosis, vaginal symptoms and skin atrophy. However, nothing in Anttila or Blom et al., either alone or in combination, teaches or suggests a method for enhancing the bioavailability of orally administered ospemifene.

A finding of obviousness requires that the prior art both suggest the invention and provide one of ordinary skill with a reasonable expectation of success. *In re O'Farrell* 853 F.2d 894, 903, 7 USPQ2d 1673 (Fed. Cir. 1988). Secondary considerations such as unexpected results must be considered if present. *Stratoflex, Inc. v. Aeroquip Corp.,* 713 F.2d 1530, 1538-39, 218 USPQ 871, 879 (Fed. Cir. 1983); *In re Merck & Co., Inc.,* 800 F.2d 1091, 1096, 231 USPQ 375, 378 (Fed. Cir. 1986).

Applicant respectfully maintains that claims 1-5 and 7-13 are not obvious under 35 U.S.C. § 103(a) over Anttila in view of Blom et al. Applicant does not concede there is a prima facie case of obviousness. Even assuming for the sake of argument that there is a prima facie case of obviousness, Applicant contends that there is sufficient rebuttal evidence to overcome the rejection.

Teaching away

The USPTO must consider rebuttal evidence of teaching away. *See In re Sullivan*, 84 USPQ2d 1034, 1038 (Fed. Cir. 2007) (The Federal Circuit remanded an appeal back to the BPAI for failure to consider rebuttal evidence put forth by the Applicant during prosecution).

As pointed out in previous replies, Anttila discloses that toremifene "can be taken equally well in fasted conditions or with meals." The t_{max} (time to peak concentration) was delayed from 2.3 hours to 4.0 hours, but the C_{max} (peak concentration), AUC (area

under the curve), and $t_{1/2}$ (half-life) values "were not significantly different" following a 14-hour fast compared to following a standard high-fat meal. In addition, the pharmacokinetic parameters for the active toremifene metabolite N-demethyltoremifene "were similar under fed and fasted conditions." Thus, Anttila would teach away from the presence of a food effect for triphenylethylenes such as ospemifene.

In accordance with *In re Sullivan*, Applicant previously requested that the teaching away of the Anttila reference be specifically addressed. The Examiner previously relied upon the Melander reference relating a food effect for dicoumarol (a totally unrelated drug) for the proposition that one would "check the bioavailability of food effect on drugs before administration." However, the Examiner has withdrawn the rejection using Melander.

In the present rejection, the Examiner acknowledges that the effect of food intake on ospemifene absorption is 2-3 times higher than in fasted state, but deems these results to be unpersuasive. The Examiner deems the data are unpersuasive because Anttila "specifically teaches administration with food." However, this reasoning is based upon an erroneous premise. Anttila teaches the administration of toremifene (the closest recognized prior art compound to ospemifene), not ospemifene, to subjects in fasted and fed states and demonstrates no food effect. It is therefore unexpected that another triphenylethylene such as ospemifene would exhibit a significant and favorable food effect as demonstrated by Applicant.

Based on the closest prior art, one of ordinary skill would have expected that administering ospemifene in combination with a foodstuff having nutritional value and causing secretion of bile acids, and taken shortly before, during or after administering ospemifene would have ***no effect*** on bioavailability of ospemifene. That is clearly not the case as shown in the results supporting Applicant's invention. Applicant respectfully requests that the Examiner reconsider the clear evidence teaching away from the claimed invention taught by Anttila.

Unexpected results

A patent applicant may also attempt to rebut a *prima facie* case of obviousness with evidence of suprising results. *See In re Peterson*, 315 F.3d 1325, 1330-1331 (Fed.

Cir. 2003). The present application discloses that the effect of food intake on ospemifene absorption is 2-3 fold higher than in the fasted state (page 4, lines 4-5). The effect of food also increases the bioavailability of ospemifene in the fed state as compared to the fasted state. (see e.g., Figures 1 and 2). The Examiner attempts to discredit the evidence of unexpected superior results by arguing that Anttila teaches the administration of an "identical" chemical composition and that one would expect "identical" compositions to have the same properties.

However, the basic premise of the Examiner's argument, i.e. that the claimed composition is identical to Anttila, is erroneous. This is not a situation where the compositions are identical and therefore their properties would be presumed to be identical. Rather, this case is an instance where the claimed chemical composition is different from the closest prior art, but demonstrates unexpectedly superior oral bioavailability over that art. The Examiner has no basis to disbelieve the data provided in the specification and no grounds to argue that the claimed invention is the same as the prior art. One of ordinary skill in the art would *not* expect the oral bioavailability of ospemifene to be enhanced by administering the drug with food. Yet, it clearly is.

Since the Anttila reference teaches away from the presently claimed invention, Applicant has presented evidence of unexpected results, and the Office has not rebutted the evidence of unexpected results, Applicant respectfully requests that the rejection under 35 U.S.C. 103(a) under Anttila in light of Blom et al. be reconsidered and withdrawn.

III. FIRST REJECTION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 1 and 8 – 9 remain rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1-12 of U.S. Patent Application No. 11/201,098 (US 2005/0272825). The Office Action alleged that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims require the compound ospemifene is administered for the treatment of skin atrophy. As evident by Vasu, drugs are known in the art to be administered, with food. With regard to Applicant's arguing that the disclosure is to

enhancing bioavailability will not change treating atrophy, because as soon as the drug is available treating will proceed."

Applicant respectfully submits that claims 1 and 8 – 9 should not be rejected for obviousness-type double patenting over the '098 patent application. For the reasons set out above in response to the rejection under 35 U.S.C. § 103(a), Applicant similarly maintains that claims 1 and 8 – 9 should not be rejected for obviousness-type double patenting, in view of the teaching away of Anttila, and the unexpected results in disclosed in the specification. Therefore, Applicant respectfully requests that the obviousness-type double patenting rejection of claims 1 and 8 - 9 over US Application No. 11/201,098 be withdrawn.

IV. SECOND REJECTION FOR OBVIOUSNESS-TYPE DOUBLE PATENTING

Claims 1 – 9 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,984,665 ("the '665 patent"). The Office Action alleged that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other. As evident by Vasu, drugs are known in the art to be administered with food."

Applicant respectfully submits that claims 1 – 9 should not be rejected for obviousness-type double patenting over the '665 patent. For the reasons set forth above in response to the rejection under 35 U.S.C. § 103(a), Applicant similarly maintains that claims 1 – 9 should not be rejected for obviousness-type double patenting, in view of the teaching away of Anttila, and the unexpected results in disclosed in the specification. Therefore, Applicant respectfully requests that the obviousness-type double patenting rejection of claims 1 – 9 over the '665 patent be withdrawn.

Applicant thanks the Examiner for her consideration of this case and submit that the case is in condition for immediate allowance. If the Examiner believes that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at 734-302-6042.

Respectfully submitted,

Dated: February 25, 2009

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